

WHAT IS CLAIMED IS:

1. 1. A method for identifying a test composition or agent which modulates the efficiency of translation termination which comprises:
 2. (a) contacting the *MTT1* with a test composition or agent under conditions permitting binding between the *MTT1* and the test composition;
 3. (b) detecting specific binding of the a test composition or agent to the *MTT1*;
 4. and
 5. (c) determining whether the a test composition or agent inhibits the *MTT1* so as to identify a test composition or agent which is which modulates the efficiency of translation termination.
1. 2. A method of identifying a test composition or agent which modulates binding to *MTT1*, the method comprising:
 2. (a) incubating components comprising the test composition, and *MTT1* wherein the incubating is carried out under conditions sufficient to permit the components to interact; and
 3. (b) measuring the effect of the test composition on the binding to *MTT1*.
1. 3. The method of claim 2, further comprising identifying a gene comprising;
 2. (a) introducing into a cell a test composition which modulates binding to *MTT1*;
 3. (b) determining the phenotype of the cell after (a);
 4. (c) comparing the cellular phenotype after (a) with the cellular phenotype before (a); and
 5. (d) identifying the gene of the cell into which the test composition has been introduced.

1 4. A method of detecting a nonsense suppression disorder associated with the
2 expression of mtt1 protein, wherein the method comprises contacting a sample
3 from a subject having or suspected of having a disorder with a reagent that detects
4 expression of the mtt1 protein and detecting the binding of the reagent in the
5 sample.

1 5. An agent which inhibits, facilitates, or modulates the helicase, ATPase activity
2 of MTT1.

1 6. The agent of claim 5, wherein the agent is a ribozyme, antisense molecule, or
2 ligand which acts as an antagonist or agonist of translation termination.

1 7. An isolated multiprotein complex comprising a MTT1 gene, human Upf1p
2 protein, a peptidyl eucaryotic release factor 1 (eRF1) and a peptidyl eucaryotic
3 release factor 3 (eRF3), wherein the complex is effective to modulate peptidyl
4 transferase activity during translation.

1 8. The complex of claim 7, further comprising human Upf3p and/or Upf2p.

1 9. An antibody which binds to the complex of claim 7.

1 10. The antibody of claim 9, wherein the antibody is a monoclonal or polyclonal

1 11. The antibody of claim 9, wherein the antibody has a label.

1 12. An agent which binds to the complex of claims 7 or 8.

1 13. An agent which inhibits or modulates the binding of human MTT1 to eRF3; or
2 MTT1 to a polysome.

- 1 14. An agent which facilitates the binding of human MTT1 to eRF3; or MTT1 to a
- 2 polysome.
- 1 15. The agent of claim 12, wherein the agent has a label or marker.
- 1 16. The agent of claim 14, wherein the agent is an antisense molecule or a ribozyme.
- 1 17. A method of modulating peptidyl transferase activity during translation,
2 comprising contacting a cell with the complex of claim 7 in an amount effective
3 to facilitate translation termination, thereby modulating the peptidyl transferase
4 activity.
- 1 18. A method of modulating peptidyl transferase activity during translation,
2 comprising contacting a cell with the agent of claim 12, in an amount effective
3 to suppress nonsense translation termination, thereby modulating the peptidyl
4 transferase activity.
- 1 19. The method of claim 18, wherein the peptidyl transferase activity during
2 translation comprises initiation, elongation, termination and degradation of
3 mRNA.
- 1 20. A method of modulating the efficiency of translation termination of mRNA at a
2 nonsense codon and/or promoting degradation of aberrant transcripts,
3 comprising contacting a cell with the agent of claim 12, in an amount effective
4 to modulate the efficiency of translation termination of mRNA at a nonsense
5 codon and/or promoting degradation of aberrant transcripts.
- 1 21. A method of screening for a drug involved in peptidyl transferase activity during
2 translation comprising: a) contacting cells with a candidate drug; and b) assaying

3 for modulation of the complex of claims 7, wherein a drug that modulates
4 complex is involved in peptidyl transferase activity.

1 22. A method of screening for a drug active involved in enhancing translation
2 termination comprising: a) contacting cells with a candidate drug; and b)
3 assaying for modulation of the protein complex of claims 7; wherein a drug that
4 modulates protein complex is involved in enhancing translation termination.

1 23. A method of screening for a drug involved in enhancing translation termination
2 comprising: a) incubating the drug and the complex; and b) measuring the effect
3 on nonsense suppression, thereby screening for a drug involved in enhancing
4 translation termination.

1 24. The method of claim 23, wherein the assay is a RNA assay or a ATPase assay.

1 25. A method of screening for a drug which inhibits the interaction between MTT1
2 and eRF3, comprising: a) contacting cells with a candidate drug; and b) assaying
3 for modulation of the complex of claim 7, wherein a drug that modulates the
4 binding of MTT1 to eRF3 is involved in enhancing translation termination.

1 26. A method of modulating the efficiency of translation termination of mRNA
2 and/or degradation of aberrant transcripts in a cell, said method comprising: a)
3 providing a cell containing a vector comprising the nucleic acid encoding the
4 complex of claim 7; or an antisense thereof; b) overexpressing said vector in
5 said cell to produce an overexpressed complex so as to interfere with the
6 function of the complex.

1 27. A method for identifying a disease state involving a defect in the complex of
2 claim 7 comprising: (a) transfecting a cell with a nucleic acid which encodes the
3 complex; (b) determining the proportion of the defective complex of the cell after

4 transfection; (c) comparing the proportion of the defective complex of the cell
5 after transfection with the proportion of defective complex of the cell before
6 transfection.

1 28. A method for treating a disease associated with peptidyl transferase activity,
2 comprising administering to a subject a therapeutically effective amount of a
3 pharmaceutical composition comprising the complex of claim 7 or the agent of
4 claim 12, and a pharmaceutical carrier or diluent, thereby treating the subject.

1 29. The method of claim 28, wherein the disease results from a nonsense or
2 frameshift mutation.

1 30. The method of claim 29, wherein the disease is β -thalassemia, β -globin,
2 Duchenne/Becker Muscular Dystrophy, Hemophilia A, Hemophilia B, Von
3 Willebrand Disease, Osteogenesis Imperfecta (OI), Breast cancer, Ovarian
4 Cancer, Wilms Tumor, Hirschsprung disease, Cystic fibrosis, Kidney Stones,
5 Familial hypercholesterolemia (FH), Retinitis Pigmentosa, or
6 Neurofibromatosis, Retinoblastoma, ATM, Costmann Disease.

1 31. A method for identifying a disease state involving defective multimeric proteins
2 comprising:

3 (a) transfecting a cell with the vector of claim ;
4 (b) determining the proportion of defective multimeric proteins of the cell
5 after tansfection;
6 (c) comparing the proportion of defective multimeric proteins of the cell after
7 transfection with the proportion of defective multimeric proteins of the
8 cell before transfection.

1 32. A method of identifying genes which are involved in modulation of translation
2 termination, which comprises: a) isolated a gene of interest; and b) determining

3 whether the gene of interest comprises motifs I-IX, wherein if the gene comprises
4 any one of the nine motifs the gene modulates translation fidelity including
5 initiation, elongation, termination, decay.

1 33. The method of claim 32, wherein the motif I comprises the sequence:
2 GppGTKTxT-X(n).

1 34. The method of claim 32, wherein the motif II comprises the sequence
2 riLxcaSNxAvDxl-X(n).

1 35. The method of claim 32, wherein the motif III comprises the sequence
2 vviDExxQaxxxxxiPi- X(n).

1 36. The method of claim 32, wherein the motif IV comprises the sequence xxil
2 aGDxxQLp- X(n).

1 37. The method of claim 32, wherein the motif V comprises the sequence lxx SLF
2 erv- X(n).

1 38. The method of claim 32, wherein the motif VI comprises the sequence
2 LxxQYRMhpxisefpxYxgxL- X(n).

1 39. The method of claim 32, wherein the motif VII comprises the sequence
2 IgvitPYxxQvxxl- X(n).

1 40. The method of claim 32, wherein the motif VIII comprises the sequence
2 vevxtVDxFQGreKdxIiIsc VR- X(n).

1 41. The method of claim 32, wherein the motif IX comprises the sequence
2 iGFLxdxRRINVaITrak.